160-90-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Supplemental Evidence and Data Request on Behavioral Interventions for Migraine Prevention

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Supplemental Evidence and Data Submissions

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public. Scientific information is being solicited to inform our review on Behavioral Interventions for Migraine Prevention, which is currently being conducted by the AHRQ's Evidence-based Practice Centers (EPC) Program. Access to published and unpublished pertinent scientific information will improve the quality of this review.

DATES: *Submission Deadline* on or before **[INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]**.

ADDRESSES:

E-mail submissions: epc@ahrq.hhs.gov

Print submissions:

Mailing Address:

Center for Evidence and Practice Improvement

Agency for Healthcare Research and Quality

ATTN: EPC SEADs Coordinator

5600 Fishers Lane

Mail Stop 06E53A

Rockville, MD 20857

Shipping Address (FedEx, UPS, etc.):

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5600 Fishers Lane

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FOR FURTHER INFORMATION CONTACT:

Jenae Benns, Telephone: 301-427-1496 or Email: epc@ahrq.hhs.gov.

SUPPLEMENTARY INFORMATION:

The Agency for Healthcare Research and Quality has commissioned the Evidence-based Practice Centers (EPC) Program to complete a review of the evidence for Behavioral Interventions for Migraine Prevention. AHRQ is conducting this systematic review pursuant to Section 902 of the Public Health Service Act, 42 U.S.C. 299a.

The EPC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on Behavioral Interventions for Migraine Prevention, including those that describe adverse events. The entire research protocol is available online at: https://effectivehealthcare.ahrq.gov/products/behavioral-interventions-migraine-prevention/protocol

This is to notify the public that the EPC Program would find the following information on Behavioral Interventions for Migraine Prevention helpful:

- A list of completed studies that your organization has sponsored for this indication. In the list, please *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number*.

        - *For completed studies that do not have results on ClinicalTrials.gov*, a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.
    - *A list of ongoing studies that your organization has sponsored for this indication*. In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
    - Description of whether the above studies constitute *ALL Phase II and above clinical trials* sponsored by your organization for this indication and an index outlining the relevant information in each submitted file.

Your contribution is very beneficial to the Program. Materials submitted must be publicly available or able to be made public. Materials that are considered confidential; marketing materials; study types not included in the review; or information on indications not included in the review cannot be used by the EPC Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EPC Program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at: https://www.effectivehealthcare.ahrq.gov/email-updates.

The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions.

Key Questions (KQ)

KQ 1: What are the benefits and harms of behavioral interventions, either alone or in combination with other preventive strategies (including pharmacologic therapy), for migraine prevention compared to inactive control for children and adults?

KQ 1a: What are the benefits and harms of behavioral interventions delivered via telehealth and digital health (e/mHealth) technology compared to inactive control?

KQ 2: What is the comparative effectiveness and harms of a behavioral intervention for migraine prevention compared to either a) a pharmacologic preventive agent or b) another behavioral intervention for children and adults?

KQ 2a: What is the comparative effectiveness and harms of behavioral interventions delivered via telehealth and digital health (e/mHealth) technology compared to a) pharmacologic prevention or b) other behavioral interventions?

KQ 3: For multicomponent or combined behavioral interventions, what are the effects of individual behavioral intervention components?

KQ 4: What are the benefits and harms of non-headache focused behavioral interventions (e.g., CBT for insomnia, CBT for depression/anxiety, parent training) for migraine prevention in children and adults with migraine?

KQ 5: For key questions 1–4, how do the findings vary by baseline biopsychosocial factors (e.g., sex, socioeconomic status, co-occurring mental health conditions)?

Contextual Questions:

CQ 1: What evidence is available on the benefits of behavioral preventive treatments for children and adults with migraine that include intervention components targeting caregivers (e.g., parents, spouses, and other key support people)?

CQ 2: What are patient and provider perceptions of the benefits, harms, and barriers to engaging with behavioral treatments for migraine prevention in children and adults?

PICOTS (Populations, Interventions, Comparators, Outcomes, Timing, and Setting)

PICOTS	Inclusion	Exclusion
Patients	**All KQs:** • Children (age 6 to 11), adolescents (12 to 17), and adults (18 or older) with migraine headache (episodic or chronic) We will not require studies to only include individuals with an International Classification of Headache Disorders diagnosis of migraine headache. • ≥80% of study participants had migraine headache, or the study reports a subgroup analysis comprised of at least 80% migraine patients • We will include studies with participants with other headache types (e.g., medication overuse headache, tension type headache, cluster headache, etc.) in addition to migraine, as long as ≥80% of participants have migraine	**All KQs:** Studies conducted exclusively • Among individuals in institutions (e.g., psychiatric inpatients, long-term care facilities, incarcerated populations) • Parents, for studies with interventions targeting children and adolescents • Individuals with psychotic disorders
Interventions	**KQs 1–3** Migraine-focused behavioral interventions used for prevention, administered either alone or with pharmacotherapy, delivered in-person, via telehealth, or with e- or mHealth 1. CBT • Cognitive behavioral therapy • Cognitive therapy • Behavioral therapy • Stress management training (SMT) • Coping skills training • "Learning to cope with triggers" (LCT) • Parent/caregiver operant training (parent or caregiver reinforces coping behaviors) • Problem-solving training 2. Biofeedback	We will exclude studies focused solely on the following interventions: • Physical therapy • Exercise • Catharsis therapy (e.g., written emotional disclosure) • Occupational therapy • Creative arts therapy (art therapy, music therapy, dance therapy)

	• Thermal/temperature biofeedback (Hand warming/Thermal biofeedback) (often feedback of skin temperature from finger) • Electromyographic (EMG) biofeedback (feedback of electrical activity from muscles of scalp, neck, or upper body) • Heart rate variability biofeedback • Electrocardio biofeedback • Pulse • Blood Volume Pulse • Respiratory • Electroencephalography (EEG)/Neurofeedback 3. Relaxation • Diaphragmatic Breathing • Progressive muscle relaxation (alternatively tensing/relaxing selected muscles) • Autogenic feedback (use of calm, self-soothing statements to promote a state of deep relaxation) • Autogenic training 4. Mindfulness based stress reduction • Meditation (use of silently repeated word or sound to promote mental calm and relaxation) • Transcendental meditation • Guided imagery/Guided visual imagery 5. Third wave CBT • Acceptance and commitment therapy 6. Education • Education (skills, lifestyle, exercise, nutrition, hydration, stress management, sleep hygiene) • Neuroscience education therapy • Healthy lifestyle counseling • Sleep counseling • Trigger avoidance • Weight management (informational) • Diary/tracking 7. Hypnotherapy 8. Trauma-informed therapy	

	• Eye movement desensitization and reprocessing (EMDR) • Trauma-focused therapy 9. Dialectical behavioral therapy (DBT) 10. Motivational interviewing and stages of change 11. Professionally led support groups/peer support 12. Combination therapies **KQ1a and KQ2a:** The above interventions delivered via telehealth or with e- or mHealth. **KQ 4** Non-headache focused behavioral interventions, e.g., • CBT for insomnia or depression/anxiety • Sleep hygiene counseling • Parent/caregiver operant training (parent or caregiver reinforces adaptive sleep behaviors) • Healthy lifestyle counseling **KQ5** Interventions included for KQs 1–4	
Comparisons	**KQs 1** • No intervention (e.g., waitlist, usual care) • Minimal intervention (e.g., educational materials without skills training) • Most active: Attention control, sham, or placebo **KQs 2–4** A different eligible behavioral intervention **KQ 2–4** Medications from the following drug classes (see Table 2): • Alpha agonists • Angiotensin-converting enzyme inhibitors/Angiotensin receptor blockers • Antiepileptics • Antihistamines (for child and adolescents only) • Beta-blockers • Botulinum toxin type A	Comparators not listed as included.

	• Calcitonin gene–related peptide antagonists • Calcium channel blockers • Other antidepressants • Serotonin norepinephrine reuptake inhibitors (SNRIs) • Tricyclic antidepressants **KQ5** Comparators in KQs 1–4	
Outcomes	**All KQs** Migraine/Headache frequency: • Migraine / headache count: Migraine days per month, migraine attacks per month, headache days per month, or headaches per month. • Responder rate: 50% or more reduction in one of the above quantities Functional Status/Disability • MIDAS, PedMIDAS, HANA, MIBS, FIS, FDI (Parent form), FDI-(child and adolescent), IMPAC) Quality of Life (QOL) • Migraine Specific: HIT-6, MSQoL v2.1, MSQ • General: SF-36, EQ-5, SF-12, PedsQL Adverse effects such as dropout and any reported Emotional Status • Anxiety symptoms (e.g., GAD-7, PROMIS Pediatric – Anxiety, HADS) • Depression symptoms (e.g., PHQ4, PHQ 9, CDI, PROMIS Pediatric-Depression, HADS) Other: • Most bothersome symptoms • Headache pain intensity (VAS, NRS) • Acute headache medication use • Discontinuation of preventive medication	

	KQ 4. Additional outcomes: • Anxiety (e.g., GAD-7, PROMIS Pediatric - Anxiety) • Depression (e.g., PHQ 4, PHQ 9, CDI, PROMIS Pediatric-Depression) • Sleep outcomes (sleep onset latency, wake after sleep onset, total sleep time, sleep efficiency)	
Study Design Criteria	**All KQs:** • Randomized controlled trials reporting outcomes for ≥ 10 participants per treatment arm • Period 1 data from crossover RCTs • Published in English-language • Published 1975 or after For KQ1-4, we will require studies to report at least one of four primary outcomes: Migraine/Headache frequency, migraine-related disability, migraine-specific quality of life, and/or adverse events.	**All KQs:** • Exclude crossover trials not reporting period 1 data separately • Exclude reviews, letters, guidelines, position statements and commentaries • Exclude single arm or non-randomized controlled studies SRs will only be used to identify potential RCTs for inclusion
Setting	• Any non-inpatient setting • Trials conducted in countries rated as "very high" on the 2022 Human Development Index (as defined by the United Nations Development Programme)	Hospitalized patients
Timing	Studies must report a primary outcome at 4 weeks or longer after treatment initiation	

CDI = Children's Depression Inventory, EQ-5D = EuroQol-5D, FDI-Child Form = Functional Disability Inventory - Child and Adolescent Form, FDI-Parent Form = Functional Disability Inventory - Parent Form, FIS = Fatigue Impact Scale, GAD-7 = General Anxiety Disorder-7, HADS = Hospital Anxiety and Depression Scale, HANA = Headache Needs Assessment, HIT–6™ = Headache Impact Test, IMPAC = Impact of Migraine on Partners and Adolescent Children, MIBS = Migraine Interictal Burden Scale, MIDAS = Migraine Disability Assessment, MSQ = Migraine Specific Quality of Life Questionnaire v. 2.1, NRS = Numeric Rating Scale, PedMIDAS = Pediatric Migraine-Specific Disability Assessment, PedsQL = Pediatric Quality of Life Inventory, PHQ = Patient Health Questionnaire–Depression, PQ-LES-Q = Pediatric quality of life enjoyment and satisfaction , SF-12 = 12-Item Short Form Survey, SF-36 = 36-Item Short Form Survey, VAS = Visual Analogue Scale

Dated: February 14, 2023.

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Associate Director.

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